

REMARKS

Claims 1-7 are pending. No amendments are presented herein. Rather, reconsideration of the application is requested in view of the following remarks.

As an initial matter, Applicants appreciate the indication of allowable subject matter, i.e., that claims 5-7 are merely objected to as being dependent on a rejected base claim, but are otherwise allowable.

Referring to the only outstanding rejection, claims 1-4 stand rejected under 35 USC §103(a) over Bertau et al. (Tetrahedron: Asymmetry 12, 2001, PP. 2103-2107) in combination with Ratovelomanana-Vidal et al. (J. Org. Chem., 567 (1998), pp. 163-171).

The Office Action refers to Bertau et al. with particularity at pages 2103-2105 and alleges that the reference teaches a process for the production of a straight chain, optically active 2-amino cyclohexanol comprising the following steps:

- enantioselective reduction of keto ester in the presence of yeast to form a 2-alkonoate cyclohexanol intermediate;
- reacting the resulting intermediate with hydrazine in the presence of alcohol such as methanol and ethanol using Curtius degradation method (to preserve the conformation of the substituents) to form a hydrazide intermediate; and
- deprotecting the amine to produce the final product, a cis-2- amino cyclohexanol.

The Office Action expressly acknowledges that Bertau et al. do not teach the selective reduction of beta keto ester on cyclohexanone, nor do they teach the use of hydrogen over ruthenium catalyst or the specific use of a benzyl alcohol.

Ratovelomanana-Videl et al. is added for its alleged teaching of a method for reducing a beta-

keto ester to a trans beta hydroxyl ester by reacting the beta keto ester with hydrogen in the presence of a ruthenium catalyst and an ethanol solvent, whereby the ketone is reduced in preference to the ester.

The rejection is traversed. The cited documents, even in combination, do not teach or suggest the processes of the present invention.

Referring first to Bertau et al., the process of converting β -hydroxy esters into hydrazides (see, e.g., 2a-e \rightarrow 3a-e; Table 2 on, page 2105) occurs by reaction in ethanol. However, alcohol is not used in the Curtius rearrangement process described at page 2105, scheme 3: 3e \rightarrow 8e. This is clear from the fact that 6e (oxazolidinone) and 7e (carboxyamino-cyclohexanol) shown in scheme 3 are produced in the presence of water. In accordance with the methods of Bertau et al, whose purpose is to obtain oxazolidinone using Curtius rearrangement, the existence of alcohol could even be problematic. Thus, it is clear that alcohol was not used in the Curtius rearrangement in Bertau et al.

Moreover, the Curtius rearrangement is a reaction to obtain isocyanate (5e of scheme 3 of Bertau et al.) from carboxylic azides (4e), and it differs from a reaction of obtaining azide compounds (3a-e of Table 2 of Bertau et al.).

In contrast, in claim 1 of the present application, Curtius rearrangement is conducted in the presence of an alcohol represented by formula (VI) to obtain alkoxycarbonyl amino cycloalcohol represented by formula (II), and then deprotecting an alkoxycarbonyl for the amino group to produce the target amino cycloalcohol represented by formula (I) at high yield.

Referring to Bertau et al. at page 2106, Table 4, the corresponding amino alcohol is obtained by hydrolysis of oxazolidinone. However, since amino cycloalcohol is soluble in water, a multitude of highly complex steps are necessary to isolate the target compound, such as saturation of reaction mixture with NaCl, extraction with ethyl acetate, removal of volatile components in vacuo,

dissolution of obtained crude material in ethanol/diethyl ether (10:1), passing through of HCl gas until completion of precipitation, concentration after filtration, etc. (Bertau et al.)

In contrast, the process recited in the present application goes through alkoxycarbonyl amino cycloalcohol of formula (II), deprotection of an alkoxycarbonyl can be carried out by reduction in organic solvent such as ethanol or tetrahydrofuran, instead of using water. By carrying out the reduction reaction in an organic solvent, it is not necessary to go through the highly complex isolation procedures as in Bertau et al. Therefore, as shown in Examples 15-17 of the present invention, the target compound can be readily isolated by simple means such as removal of the solvent or concentration, and filtration.

As indicated above, the method of conducting Curtius rearrangement in the presence of an alcohol to obtain alkoxycarbonyl amino cycloalcohol represented by formula (II), and obtaining amino cycloalcohol of formula (I) by deprotection is not taught or even suggested in Bertau et al. Still further, the present invention offers great benefit in terms of isolating the target compound by relatively simple means.

Referring now to Ratovelomanana-Videl et al., that document cannot remedy the deficiencies of Bertau et al. For instance, Ratovelomanana-Videl et al. merely disclose the compound represented by formula (IV), which is the starting material of the present invention. Ratovelomanana-Videl et al. do not teach or suggest the present method of conducting Curtius rearrangement in the presence of above mentioned alcohol to obtain alkoxycarbonyl amino cycloalcohol represented by formula (II), and obtaining amino cycloalcohol of formula (I) by deprotection.

Therefore, even assuming *arguendo* that one skilled in the art were to combine the teachings of the cited references, one would still not arrive at the methods of the present invention.

Obviousness can only be established by modifying (or combining) the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or

motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art [See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992)].

Accordingly, reconsideration and withdrawal of the rejections are requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,



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